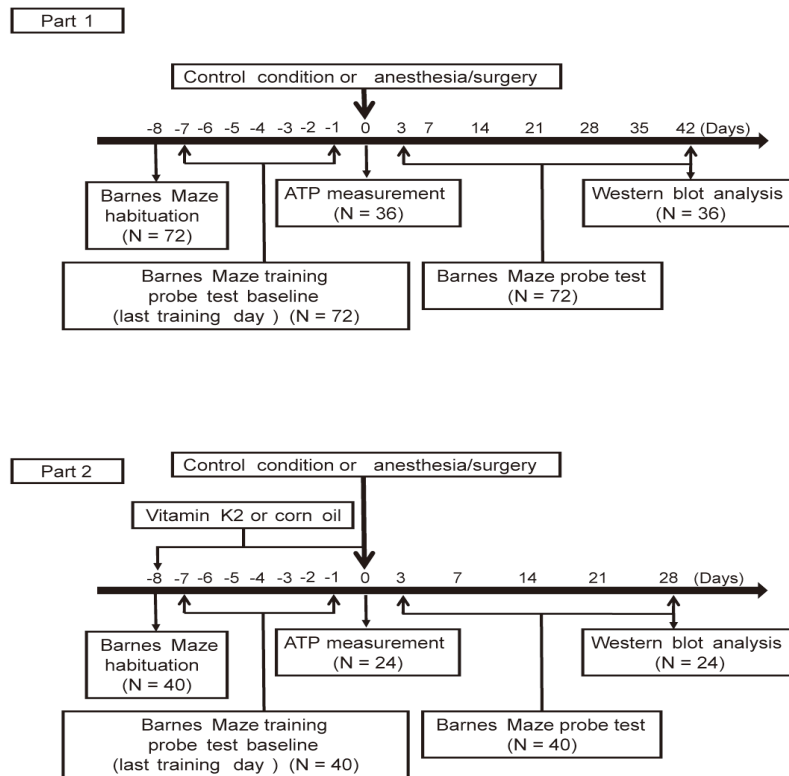


**Supplementary information.**

**Anesthetic isoflurane or desflurane plus surgery differently affect cognitive function  
in Alzheimer's disease transgenic mice**

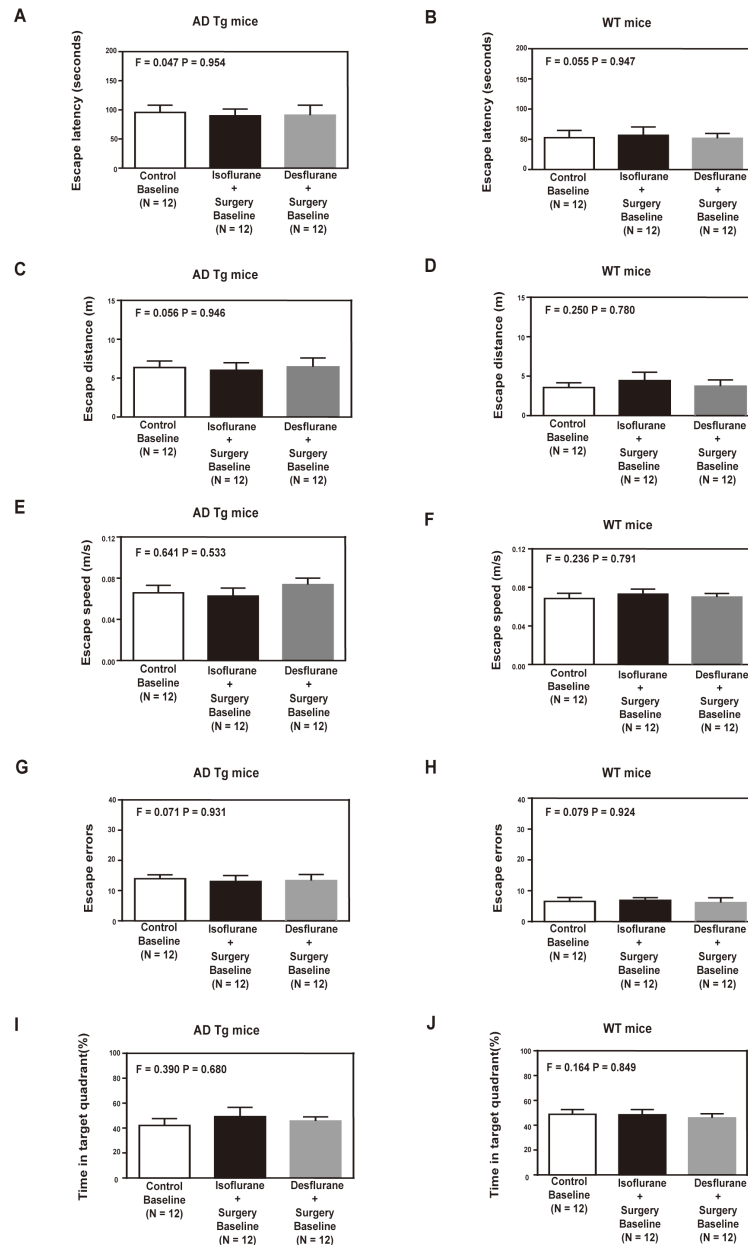
Huihui Miao, Yuanlin Dong, Yiyang Zhang, Hui Zheng, Yuan Shen, Gregory Crosby,  
Deborah J. Culley, Edward R. Marcantonio and Zhongcong Xie

## Supplementary Figure 1.



**Supplementary Figure 1. Diagram of the experimental design. Part 1.** The mice received Barnes Maze training from day 7 to day 1 (-7 to -1) before isoflurane or desflurane anesthesia plus the abdominal surgery (anesthesia/surgery). The values of the escape latency, escape distance, escape speed, escape errors and the time in target quadrant on the last day of Barnes Maze training serve as the baseline of Barnes Maze probe test. Then, the mice received Barnes Maze probe test on day 3, 7, 14, 21, 28, 35 and 42 after the anesthesia/surgery, respectively. Western blot analysis was performed at the end of the behavior tests on day 42. ATP measurement was performed immediately after the anesthesia/surgery on day 0. **Part 2.** Vitamin K2 treatment (100 mg/kg, daily) started 8 days before the anesthesia/surgery. Western blot analysis was performed after the behavior tests on day 28. ATP measurement was performed immediately after the anesthesia/surgery on day 0.

## Supplemental Figure 2.



**Supplementary Figure 2. Effects of isoflurane or desflurane plus surgery on baseline escape latency, escape distance, escape speed, escape errors and time in quadrant of Barnes Maze test in AD Tg or WT mice.** One-way ANOVA showed no significant difference between isoflurane plus surgery or desflurane plus surgery versus control condition on escape latency (**A** and **B**), escape distance (**C** and **D**), escape speed (**E** and **F**), escape errors (**G** and **H**) and time in target quadrant (**I** and **J**) of Barnes maze baseline performance in AD Tg (**A**, **C**, **E**, **G** and **I**) or WT (**B**, **D**, **F**, **H** and **J**) mice. ANOVA, analysis of variance; AD, Alzheimer's disease; Tg, transgenic; WT, wild-type. N = 12 in each group.

## Supplementary Table 1.

**Supplementary Table 1. Effects of isoflurane or desflurane plus surgery on cognitive function in AD Tg and WT mice**

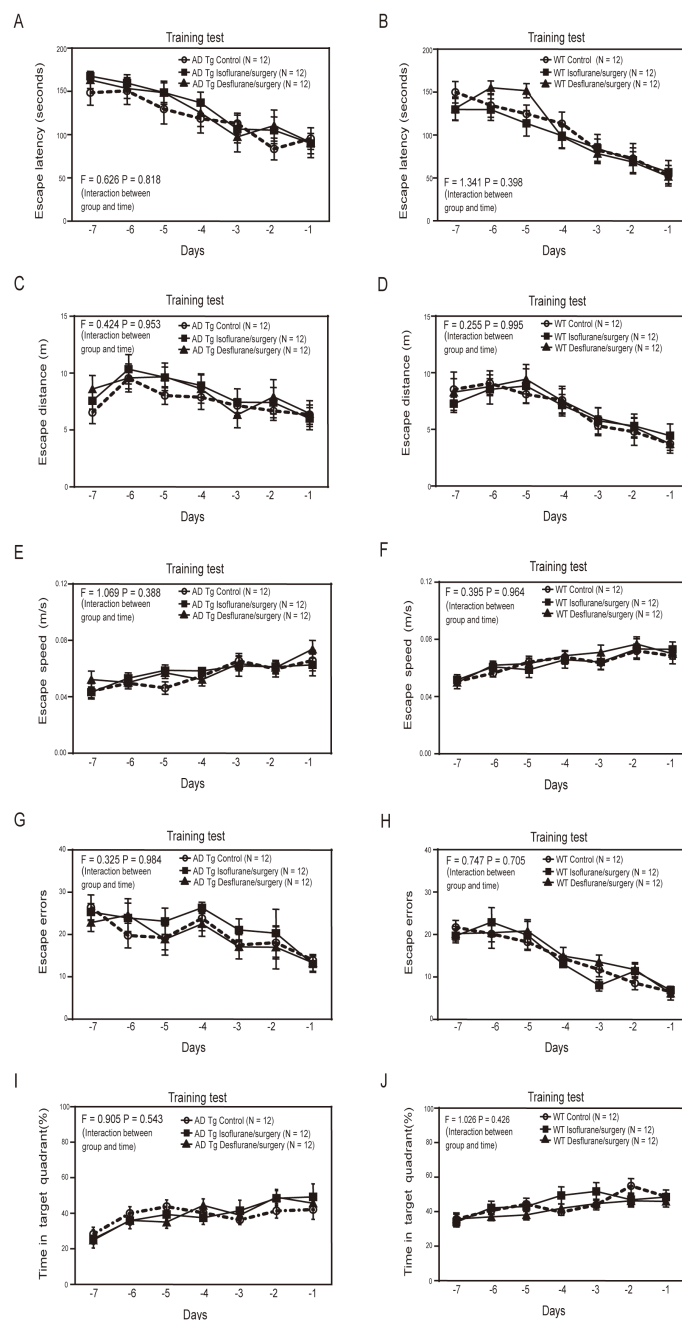
	Escape latency				Escape distance			
	AD Tg mice		WT mice		AD Tg mice		WT mice	
	Control vs Isoflurane/surgery	Control vs Desflurane/surgery	Control vs Isoflurane/surgery	Control vs Desflurane/surgery	Control vs Isoflurane/surgery	Control vs Desflurane/surgery	Control vs Isoflurane/surgery	Control vs Desflurane/surgery
D-1	0.999	0.999	0.999	0.999	0.999	0.999	0.999	0.999
D3	0.438	0.376	0.274	0.361	0.999	0.999	0.999	0.999
D7	<b>0.059</b>	0.125	0.646	0.999	<b>0.092</b>	0.591	0.999	0.999
D14	0.999	0.999	<b>0.088</b>	0.315	0.999	0.381	0.193	0.907
D21	0.999	0.999	0.141	0.999	0.916	0.335	0.784	0.999
D28	<b>*0.034</b>	0.322	0.999	0.999	<b>*0.011</b>	0.674	0.999	0.999
D35	0.999	0.999	0.999	0.999	0.317	0.112	0.999	0.933
D42	0.999	0.334	0.873	0.999	0.447	0.548	0.999	0.999

(N = 12 in each group)

\*Adjusted  $P < 0.05$

**Supplementary Table 1. Effects of isoflurane or desflurane plus surgery on cognitive function in both AD Tg and WT mice. Left part:** Isoflurane plus surgery increased the escape latency in the Barnes Maze probe test as compared to control condition on day 28 after the anesthesia/surgery in AD Tg mice ( $P = 0.034$ ). Isoflurane plus surgery induced a borderline increase in escape latency in the Barnes Maze probe test as compared to control condition on day 7 after the anesthesia/surgery in AD Tg mice ( $P = 0.059$ ). Finally, Isoflurane plus surgery induced a borderline increase in escape latency in the Barnes Maze probe test as compared to control condition on day 14 in WT mice ( $P = 0.088$ ). Desflurane plus surgery did not increase the escape latency as compared to the control condition in either AD Tg or WT mice. **Right part:** Isoflurane plus surgery increased the escape distance in the Barnes Maze probe test as compared to control condition on day 28 after the anesthesia/surgery in AD Tg mice ( $P = 0.011$ ). Desflurane plus surgery did not increase the escape distance as compared to the control condition in either AD Tg or WT mice. AD, Alzheimer's disease; Tg, transgenic; WT, wild-type. N = 12 in each group.

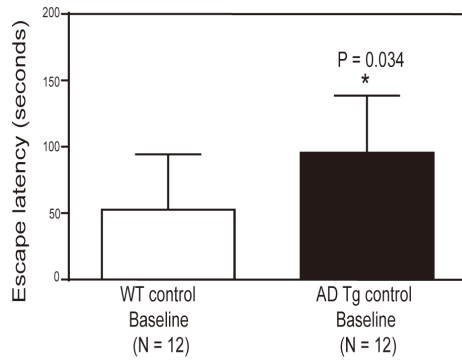
## Supplemental Figure 3.



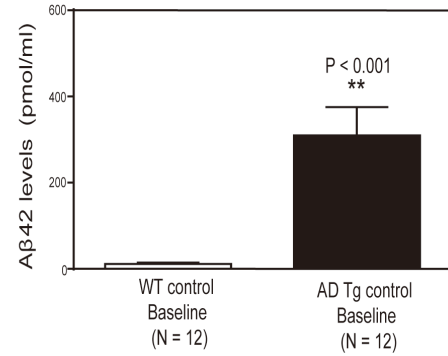
**Supplemental Figure 3. Escape latency, escape distance, escape speed, escape errors and time in target quadrant of Barnes Maze training test in AD Tg and WT mice.** Two-way ANOVA with repeated measurement showed that no significant interaction of mice in the group (isoflurane plus surgery or desflurane plus surgery or control condition) and time (days) on escape latency (**A** and **B**), escape distance (**C** and **D**), escape speed (**E** and **F**), escape errors (**G** and **H**) and time in target quadrant (**I** and **J**) in AD Tg (**A**, **C**, **E**, **G** and **I**) and WT (**B**, **D**, **F**, **H** and **J**) mice. ANOVA, analysis of variance; AD, Alzheimer's disease; Tg, transgenic; WT, wild-type. N = 12 in each group.

# Supplementary Figure 4.

A

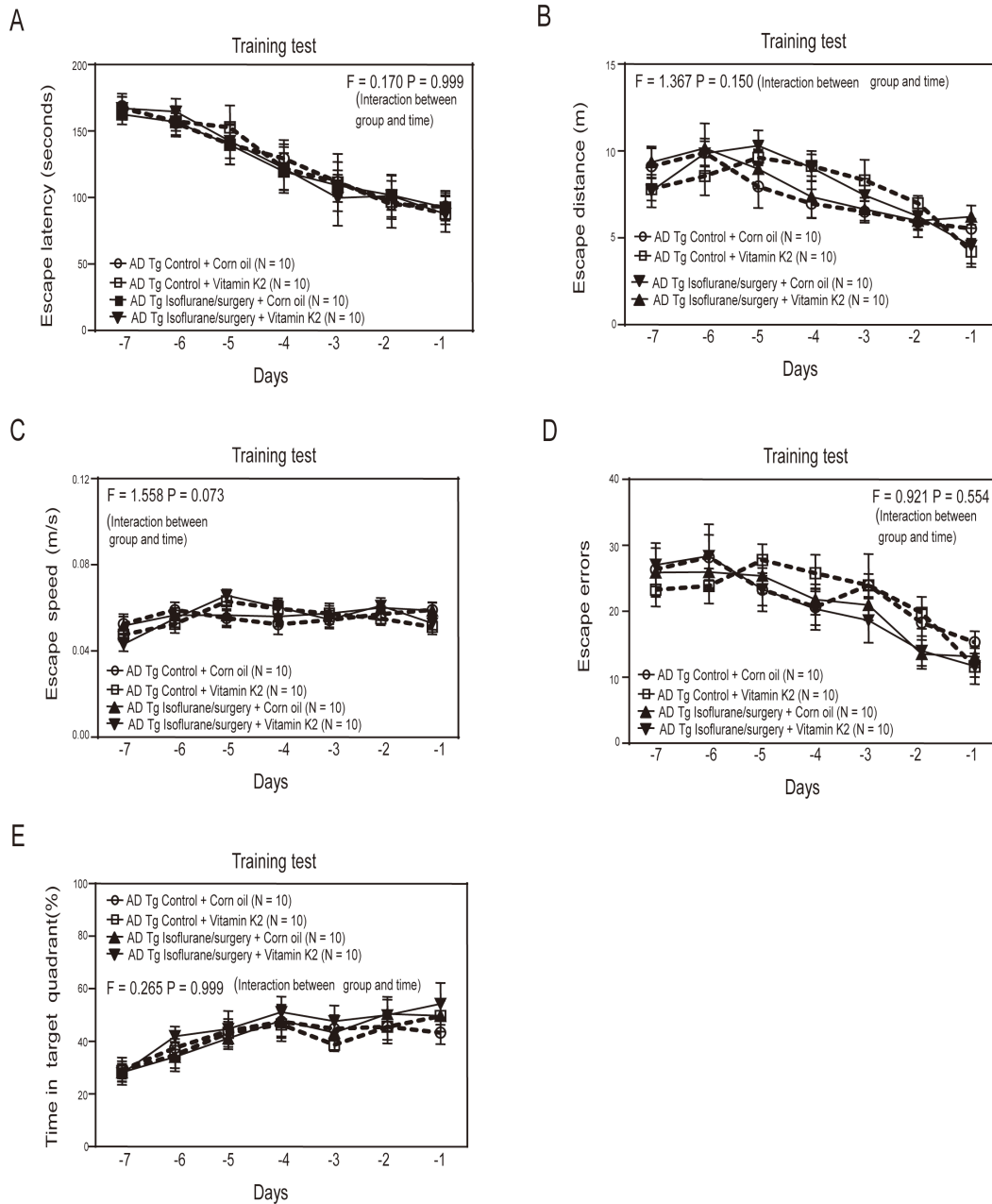


B



**Supplementary Figure 4. The comparison of the baseline of escape latency in Barnes Maze probe test and Aβ42 levels in the brain tissues between AD Tg control and WT control mice. A.** The baseline of escape latency in Barnes Maze probe test of AD Tg control mice was significant longer than that of WT control mice at one day (day -1) before the anesthesia/surgery ( $P = 0.034$ ). **B.** The Aβ42 levels of cortex of AD Tg control mice were significantly higher than that of WT control mice ( $P < 0.001$ ). AD, Alzheimer's disease; Tg, transgenic; WT, wild-type; Aβ, β-amyloid protein. N = 12 in each group.

## Supplementary Figure 5.



**Supplementary Figure 5. Effects of isoflurane plus surgery on escape latency, escape distance, escape speed, escape errors and time in target quadrant of Barnes Maze training test in AD Tg mice with pretreatment of corn oil or Vitamin K2.** Two-way ANOVA with repeated measurement showed no significant interaction of group (isoflurane plus surgery versus control condition) and time (days) on escape latency (A), escape distance (B), escape speed (C), escape errors (D) and time in target quadrant (E) of Barnes maze training test in AD Tg mice with pretreatment of corn oil or Vitamin K2. ANOVA, analysis of variance; AD, Alzheimer's disease; Tg, transgenic; WT, wild-type. N = 10 in each group.